

RING-OPENING POLYMERIZATION OF L-LACTIDE WITH RARE EARTH ARYLOXIDES SUBSTITUTED BY VARIOUS ALKYL GROUPS*

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Abstract Rare earth aryloxides substituted by various alkyl groups $[\text{Ln}(\text{OAr})_3]$ such as methyl, isopropyl and tertbutyl, were used as single component catalysts to affect ring-opening polymerization of L-lactide (LLA). The catalytic activity, polymerization characteristics, polymerization kinetics and the mechanism were studied. It was found that the catalytic activity of rare earth aryloxides is influenced by both the structure and the number of alkyl groups on the phenyl ring. The stronger the electron-donation ability of the alkyl group, the higher the catalytic activity will be. An increase in the number of the substitute group will result in a higher catalytic activity. Lanthanum tris(2,4,6-tri-*tert*-butylphenolate) $[\text{La}(\text{OTTBP})_3]$ exhibits the highest activity among all lanthanum aryloxides. According to the ^1H -NMR data, it was proposed that the LLA polymerization proceeded *via* a coordination-insertion mechanism involving cleavage of acyl-oxygen bond of the lactide.

Keywords: Ring-opening polymerization; L-lactide; Rare earth aryloxides.

INTRODUCTION

Recent concerns with our environment call for the development of benign materials. Among all the aliphatic polymers, poly(L-lactide) (PLLA) is one of the most promising polymers attracted considerable interest in recent years. PLLA is recognized as an important material for its special applications in the biomedical, pharmaceutical and agricultural fields^[1–3] due to its biocompatibility and biodegradability. Polylactide is prepared by both direct condensation of lactic acid and ring-opening polymerization of lactide^[4–6]. However, it is very difficult to obtain polymers with high molecular weight because the direct condensation is an equilibrium reaction. Ring-opening polymerization is a convenient and efficient route to prepare polylactide, which is derived from renewable resources (*e.g.*, sugar beets, dairy products and corns). PLLA can be degraded into hydroxyacids which can be metabolized in many cases. The rapidly growing interest in biodegradable materials has also increased attention in development of efficient catalysts for ring-opening polymerization of lactides. A variety of organometallic compounds containing tin^[7], aluminum^[8–10], zinc^[11], calcium^[12, 13], magnesium^[14, 15] and iron^[16], *etc.* have been developed for LLA polymerization. However, complete removal of the catalyst residues from the polymer is not possible, and therefore low toxicity catalysts should be required for the purpose of biomedical applications, among which lanthanide-based catalysts^[17, 18] have received much attention because of their high activity, low toxicity and allowed a controlled polymerization of cyclic esters.

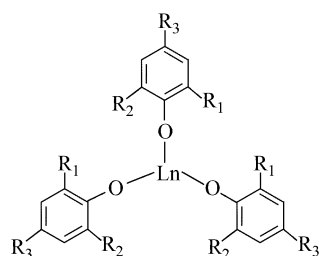
In this paper, we have successfully developed six different rare earth aryloxides and discussed the relation between the structure and catalytic activity of rare earth aryloxides, with emphasis on the polymerization characteristics, kinetics and mechanism of LLA initiated by $\text{Ln}(\text{OAr})_3$ (Scheme 1).

* This work was supported by the Natural Science Foundation of Shanxi Province (No. 2006011069) and the Opening Foundation of Key Laboratory of Shanxi Province (No. 2009011059-7).

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Received May 5, 2009; Revised June 3, 2009; Accepted June 9, 2009

doi: 10.1007/s10118-010-9065-2



Scheme 1 Structure of $\text{Ln}(\text{OAr})_3$ ($\text{Ln} = \text{La, Nd, Sm, Gd, Er}$)

Catalyst 1: $\text{R}_1 = \text{R}_2 = \text{R}_3 = \text{'Bu}$	Catalyst 2: $\text{R}_1 = \text{R}_2 = \text{'Bu}$	$\text{R}_3 = \text{H}$
Catalyst 3: $\text{R}_1 = \text{R}_2 = \text{'Pr}$	$\text{R}_3 = \text{H}$	Catalyst 4: $\text{R}_1 = \text{R}_2 = \text{H}$
Catalyst 5: $\text{R}_1 = \text{R}_2 = \text{H}$	$\text{R}_3 = \text{'Pr}$	Catalyst 6: $\text{R}_1 = \text{R}_2 = \text{H}$
		$\text{R}_3 = \text{Me}$

EXPERIMENTAL

Materials

LLA was synthesized from L-lactic acid as previously described^[19]. The crude product was recrystallized three times from ethyl acetate. Toluene and tetrahydrofuran (THF) were dried by refluxing over benzophenone-sodium complex, and distilled before use. CH_2Cl_2 and CCl_4 , dried over P_2O_5 , were also distilled. Methanol was used without further purification.

Catalyst Preparation

All catalyst preparations were performed with Schlenk tubes and a vacuum-line technique under purified nitrogen. Anhydrous rare earth chlorides were prepared from their oxides^[20]. $\text{Ln}(\text{OAr})_3$ were synthesized by the method of Ref. [21]. The concentrations of rare-earth ions in the catalyst solution were determined by titration with EDTA.

Polymerization

Polymerizations were run in 20 mL glass ampoules under nitrogen atmosphere free of moisture and oxygen. Monomer and solvent were added into the ampoules successively and prewarmed in oil bath to certain temperature. Then the catalyst solution was injected by a syringe. After certain reaction time, the polymerization was terminated by cold methanol containing 5% HCl. The obtained product was precipitated and kept in methanol for 24 h, then filtrated and washed with methanol several times. The purified PLLA was dried in vacuum at 40°C.

Measurements

^1H -NMR spectra of PLLA was recorded in CDCl_3 on a Bruker AV-400MHz spectrometer at room temperature and with tetramethylsilane (TMS) as internal standard. The number average molecular weight (M_n) and molecular weight distribution (MWD) were determined by gel permeation chromatography (PL-GPC220). The instrument was equipped with a refractive index detector and a set of columns (PL gel 10 μm MIXED-B 300 mm $\times$ 7.5 mm, PL gel 10 μm Guard 50 mm $\times$ 7.5 mm). Tetrahydrofuran (THF) was used as a mobile phase with a flow rate of 1.0 mL/min. The measurements were carried out at 40°C. Narrow polystyrene standards were used for calibration. Differential scanning calorimetric (DSC) curves were performed with a DSC (204F1) instrument by using a heating rate of 10 K/min from 60°C to 200°C.

RESULTS AND DISCUSSION

Characteristics of Polymerization

Six kinds of lanthanum aryloxides substituted by alkyl groups as initiators were separately utilized to examine the activity of various rare earth aryloxides for the LLA ring-opening polymerization in toluene, as listed in

Table 1. The sequence of catalytic activity and the prepared PLLA molecular weight are as follows: catalyst 1 > catalyst 2 > catalyst 3 > catalyst 4 > catalyst 5 > catalyst 6. Lanthanum tris(2,4,6-*tert*-butylphenolate)s [La(OTTBP)₃] (catalyst 1), showing the highest activity, can prepare PLLA over 98.6% yield with M_n of about 6.60×10^4 . Experimental results indicate that activity of lanthanum aryloxides La(OAr)₃ is significantly affected by both the donation-electronic inductive effect and number of alkyl groups on phenyl rings. The catalytic activity of La(OAr)₃ strengthens with the increasing of electron-donating ability of alkyl groups adjacent to phenyl ring. Moreover, the more the numbers of substituted alkyls on phenyl ring, the higher the catalytic activity. It should be assumed that donor effect will raise electron density on oxygen atom in six complexes facilitating ArO[−] nucleophilic attack on carbonyl carbon of the LLA monomer. This attack will increase catalytic efficiency of lanthanum aryloxides.

Table 1. Influence of different aryloxide ligands on the LLA polymerization

Initiator	[LLA] (mol/L)	[LLA]/[La] (molar ratio)	Conversion (%)	$M_n \times 10^{-4}$	MWD
Catalyst 1	1.5	1000	98.6	6.60	1.68
Catalyst 2	1.5	1000	95.5	5.92	1.77
Catalyst 3	1.5	1000	89.4	3.46	1.37
Catalyst 4	1.5	1000	88.0	3.43	1.64
Catalyst 5	1.5	1000	85.2	2.48	1.37
Catalyst 6	1.5	1000	81.3	1.96	1.59

Conditions: 70°C, 70 min, toluene

Rare earth tris(2,4,6-*tert*-butylphenolate)s [Ln(OTTBP)₃] were selected as the catalyst for further investigation of LLA polymerization characteristics because La(OTTBP)₃ exhibited the excellent activity among the six distinct aryloxide complexes. The influence of different rare earth compounds on the polymerization is summarized in Table 2. The experimental results showed that Ln(OTTBP)₃ complexes were proved as an efficient single component catalyst for LLA homopolymerization. The activity sequence of the various rare earth catalysts is: La > Sm > Gd > Nd > Er, which may result from different coordination abilities of these rare earth elements with the monomer. Larger rare earth ions easily coordinate with LLA monomer when the monomer inserts into the La—O bond of the catalyst. At the same time, a rare earth compound formed by d and s orbital electrons is more effective for the LLA polymerization than that formed by an f orbital electron, for example, Gd > Nd, although the radius of Gd³⁺ is smaller than that of Nd³⁺. Further investigation is in process.

Table 2. Effect of different rare earth aryloxides on polymerization

Ln(OTTBP) ₃	[LLA]/[Ln] (molar ratio)	Conversion (%)	$M_n \times 10^{-4}$
La	1000	98.6	6.60
Sm	800	97.6	5.68
Gd	500	97.1	6.32
Nd	300	96.8	5.11
Er	200	3.62	—

Conditions: [LLA] = 1.5 mol/L, 70°C, 70 min, toluene

Table 3 gives the influences of various solvents on the polymerization. It can be seen that LLA can be polymerized in all the solvents used. The polymerization in a non-polar solvent is more rapid and easier to give a higher molecular weight and yield than those in a polar solvent.

Table 3. Influence of different organic solvents on polymerization

Solvent	Temperature (°C)	Conversion (%)	$M_n \times 10^{-4}$
Toluene	70	98.6	6.60
CCl ₄	100	97.3	6.06
CH ₂ Cl ₂	70	87.7	5.15
THF	70	60.0	4.88

Conditions: [LLA] = 1.5 mol/L, [LLA]/[La] = 1000 molar ratio, 70 min

The effects of initiator concentration and monomer to initiator ([LLA]/[La]) molar ratio on the LLA polymerization with La(OTTBP)₃ in toluene are shown in Table 4. As seen in Table 4, PLLA with a yield above 98.6% and molecular weight of 6.60×10^4 is obtained at the monomer concentration of 1.5 mol/L and [LLA]/[La] molar ratio of 1000. The higher are the monomer concentration and initiator concentration, the broader is the molecular weight polydispersity of PLLA formed.

Table 4. Effect of LLA concentration and initiator amount on the polymerization

[LLA]	[LLA]/[La] (molar ratio)	Conversion (%)	$M_n \times 10^{-4}$	MWD
1.0	1000	96.8	5.17	1.68
1.5	1000	98.6	6.60	1.68
2.5	1000	95.9	6.33	1.70
3.0	1000	95.3	4.88	1.86
1.5	600	96.2	5.33	1.63
1.5	800	96.7	5.53	1.68
1.5	1200	96.3	5.42	1.57
1.5	1500	96.1	5.08	1.38

Conditions: 70°C, 70 min, toluene

Polymerization temperature and time have a significant influence on the polymerization, as listed in Table 5. It can be seen from the results that 70°C is the optimum temperature for LLA polymerization. Increasing reaction temperature leads to a more rapid polymerization, and PLLA is easily degraded. With further prolongation of the reaction time, the lower molecular weight and broader molecular weight polydispersity are formed because the usually slow transesterification is not negligible after reaching the reaction equilibrium. Therefore, the optimum conditions for the polymerization of LLA by La(OTTBP)₃ are as follows: [LLA] = 1.5 mol/L, [LLA] = 1000 molar ratio, 70°C, 70 min, in toluene.

Table 5. Effect of reaction temperature and time on the polymerization of LLA

Temperature (°C)	Time (min)	Conversion (%)	$M_n \times 10^{-4}$	MWD
70	50	94.9	3.86	1.69
70	60	95.1	5.15	1.68
70	70	98.6	6.60	1.72
70	80	90.6	5.47	1.77
70	90	89.3	4.51	1.83
80	70	96.5	6.43	1.59
90	70	95.7	5.72	1.74
100	70	93.4	5.16	1.81

Conditions: [LLA] = 1.5 mol/L, [LLA]/[La] = 1000 molar ratio, toluene

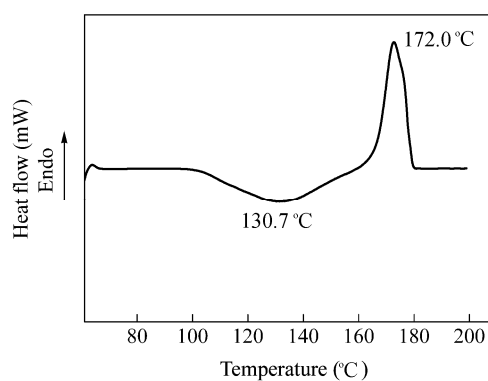


Fig. 1 DSC thermogram (second scan) of PLLA

The thermal property of the PLLA is analyzed by DSC. Figure 1 shows the second heating of the polymer sample. It is noticed that PLLA sample has an exothermic peak of crystallization at 130.7°C and an endothermic peak at 172.0°C. This is in consistent with the thermal behavior of optically pure PLLA reported by other authors^[22].

Kinetics of the Polymerization

Similar kinetic behaviors were observed in all the La(OAr)₃ systems. As an example, the kinetics of the LLA polymerization in toluene catalyzed by La(OTTBP)₃ has been investigated. A straight-line relationship holds for $\ln([LLA]_0/[LLA]_t)$ as a function of reaction time t at conversions below 20%. Figure 2 shows the time dependence of $\ln([LLA]_0/[LLA]_t)$ at four different catalyst concentrations is linear, where $[LLA]_0$ and $[LLA]_t$ are the monomer concentrations at time zero (t_0) and t , respectively. Figure 3 illustrates the correlation of polymerization rate versus concentration of La(OTTBP)₃ ($\ln R_p$ versus $\ln[La]$). From these data, it can be concluded that the polymerization rate is first order with respect to the monomer concentration and catalyst concentration, respectively. Therefore, the polymerization of LLA initiated by La(OTTBP)₃ proceeds according to the overall kinetic law of the form:

$$R_p = k_p[LLA][La(OTTBP)_3]$$

where k_p is the polymerization rate constant. The relationship between the $\ln R_p$ and the reciprocal of polymerization temperature ($1/T$) has been plotted (Fig. 4). According to the Arrhenius equation, the apparent activation energy is 57.4 kJ/mol.

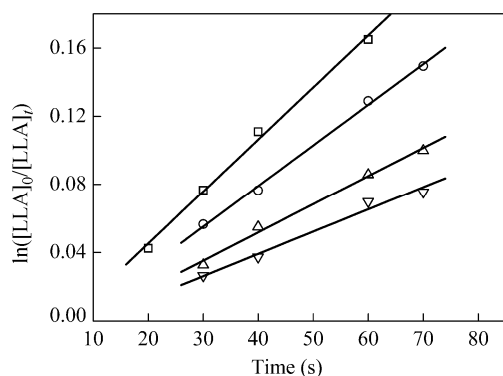


Fig. 2 $\ln([LLA]_0/[LLA]_t)$ versus time plot different catalyst concentration

Conditions: $[LLA] = 1.5$ mol/L, 70°C, toluene

□ $[La] = 2.50 \times 10^{-3}$ mol/L; ○ $[La] = 1.88 \times 10^{-3}$ mol/L

△ $[La] = 1.50 \times 10^{-3}$ mol/L; ▽ $[La] = 1.00 \times 10^{-3}$ mol/L

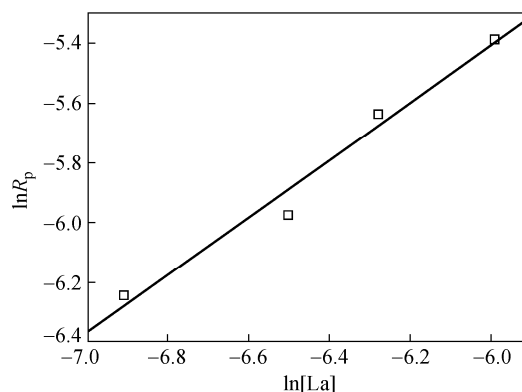


Fig. 3 Correlation of $\ln R_p$ with $\ln[La]$

Conditions: $[LLA] = 1.5$ mol/L, 70°C, toluene

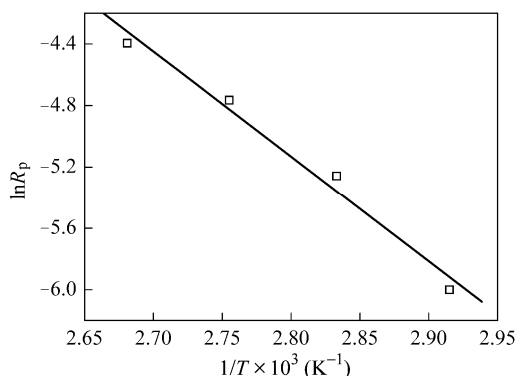


Fig. 4 Plot of $\ln R_p$ versus $1/T$

Conditions: $[LLA] = 1.5$ mol/L, $[LLA]/[La] = 1000$, toluene

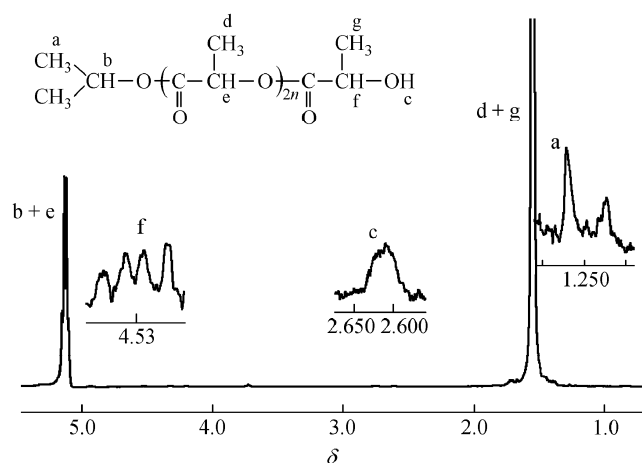
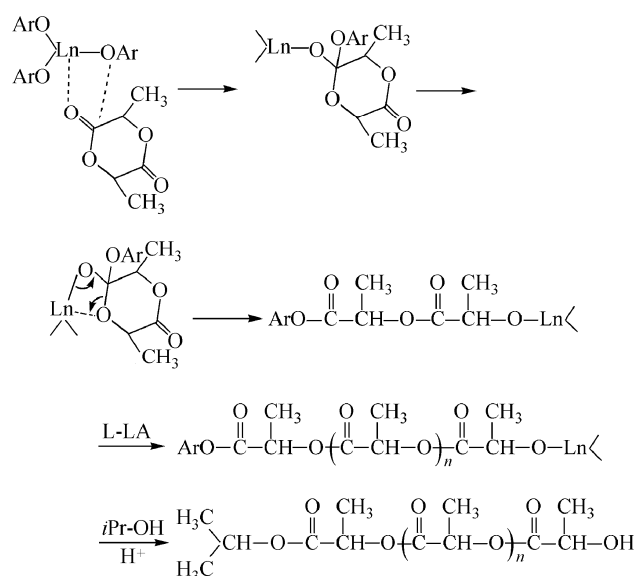


Fig. 5 ^1H -NMR of PLLA terminated by isopropanol



Scheme 2 Mechanism of the polymerization of LLA catalyzed by $\text{Ln}(\text{OAr})_3$

Mechanistic Aspects

It is difficult to clarify a differentiation between a propagation involving alkyl-oxygen cleavage and acyl-oxygen cleavage via kinetics methods. In order to identify the reaction mechanism of polymerization, a low molecular weight PLLA sample terminated by isopropanol was prepared, and its ^1H -NMR spectrum is shown in Fig. 5. From the spectrum, the chemical shifts (δ) at 5.13 and 1.55 should be assigned to the main chain protons ^eH and ^dH , respectively. Two ends of the polymer chain are $-\text{COOCH}(\text{CH}_3)_2$ group and $-\text{CH}(\text{CH}_3)\text{OH}$ group, respectively, which are confirmed by proton signals at $\delta = 1.25$ (doublet) for ^aH and $\delta = 4.53$ (multiplet) for ^fH . Therefore, it can be concluded that the LLA monomer inserts into the $\text{Ln}-\text{O}$ bond *via* selective acyl-oxygen bond scission (Scheme 2).

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